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Pages: 3 (including cover sheet)

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Date: December 3, 2003

CC:

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Dear Examiner Zara:

I sorry you did not receive the pages you requested from the Reply and Amendment filed on August 25, 2003, for 09/490,609. I am faxing them to you with this cover sheet, and I will call you to see if you have received them.

09/490,609

permitting specific nucleic acid hybridization". Therefore, Applicants submit that the claim as amended is definite.

2. On page 4, the Office rejected Claim 25 as being unclear due to the term complementary nucleic acid molecule. Applicants have amended Claim 25 to remove the term "complementary", and therefore submit that the amended claim is definite.

3. In Claim 31, the Office argues that the term "substantially hybridizes" is vague, and requests clarification. Applicants submit that the term "substantially hybridizes" is defined on page 9, lines 5-9 of the specification as follows:

"The term "substantially hybridizes" means that two nucleic acid molecules can form an anti-parallel, double-stranded nucleic acid structure under conditions (e.g. salt and temperature) that permit hybridization of sequences that exhibit 90% sequence identity or greater with each other and exhibit this identity for at least a contiguous 50 nucleotides of the nucleic acid molecules."

4. In Claim 31, the Office argues that the term "determining" does not set forth a positive step. Applicants have replaced the term with "detecting", and therefore submit that the amended claim is definite.

5. Claim 32 has been amended to provide proper claim construction from the antecedent term "hepatocyte".

Rejections under 35 U.S.C. § 102

A. Amended Claims 31 and 32 and dependent Claim 33 are not anticipated

On page 5 of the Office Action, Claims 31-35 were rejected as being anticipated by Hillman et al. Claims 34-35 are cancelled. Applicants have amended Claims 31-32 to read on SEQ NOs: 280, 384, and 488. Claim 33 is dependent on Claim 32. Applicants further submit that Hillman *et al.* does not disclose SEQ NOs: 280, 384, and 488. Because present claims 31 and 32 as amended do not read on subject matter disclosed in Hillman *et al.*, Applicants request that the 102 (e) rejection in light of Hillman be withdrawn.

On page 5 of the Office Action, Claims 31-35 were rejected as being anticipated by Upton *et al.* Applicants have amended Claims 31-32 to read on SEQ NOs: 280, 384, and 488. Claim 33 is dependent on Claim 32. Applicants further submit that Upton *et al.* does not disclose SEQ NOs: 280, 384, and 488. Because present claims 31 and 32 as

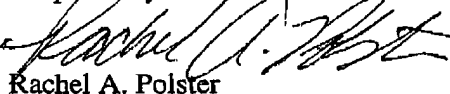
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amended do not read on subject matter disclosed in Upton *et al.*, Applicants request that the 102 (b) rejection in light of Upton be withdrawn.

On page 6 of the Office Action, Claims 31-35 were rejected as being anticipated by Lee *et al.* Applicants submit that the sequence disclosed in Lee *et al.* were not correlated with the effects of toxic compounds on gene expression and cancer progression. Rather, Lee *et al.* describes the over-expression of ESTs from PC-12 cells (from a rat pheochromocytoma cell line) in response to treatment with nerve growth factor to induce the acquisition of a neuronal phenotype, and the last paragraph on page 8307 suggests that "Application of the comparative EST approach can be readily extended to other cellular processes, such as development, homeostasis, cell-cycle regulation, apoptosis, cancer progression, and toxicological effects of drugs on gene expression." Claims 31 and 32 are directed towards the differential mRNA expression in hepatocytes in response to treatment with a compound to determine carcinogenicity. Applicants submit that Claims 31 and 32 do not read on the subject matter disclosed in Lee *et al.*, and therefore request that the 102 (b) rejection in light of Lee *et al.* be withdrawn.

In view of the foregoing amendments and remarks, Applicants believe that all claims now active in the present application are in condition for allowance. Therefore, passage of the application and claims to issue is requested. If the Examiner has any further comments or concerns, he is welcome to contact Applicants at the number below.

Respectfully submitted,



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